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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,488	ILAN ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/10/03+08/02/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *1-49 and 61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-60 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/19/03+06/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group V and HCV viral infection, in the reply filed on 08/02/2005 is acknowledged.

Applicant traversed the restriction requirement by asserting that a search for the subject matter of Groups I-V does not constitute as a serious burden for the Examiner because the groups are related in their use of metabolites for treating diseases.

Applicant's submission has been considered, however, it is not found persuasive. In the instant, the invention of Group I is directed at the administration of an **intermediary metabolite** to treat a disease, the invention of Group II is directed at the use of a **reagent** to treat a disease, and the invention of Group V is directed at the use of a mammalian **metabolite** to treat a disease. While it is recognized that teach of these inventions are directed at a method of treating a disease, however, the inventions are distinct from one another based on the material that is used in each of the inventions. The invention of Group I employs the administration of an intermediary metabolite. The invention of Group II employs the administration of a reagent, and the invention of Group V employs the administration of a mammalian metabolite. A search for a reagent that treats a disease does not equate to a search for a mammalian metabolite that treats a disease or an intermediary metabolite that treats a disease. In the instant, each of the listed inventions requires different fields of search. The search for the invention of Group I includes an intermediary metabolite, whereas the search for the invention of Group II and III would include the terms reagent and mammalian

metabolite. And a search for all terms would necessarily impose serious burden on the Office.

Furthermore, the inventions of Groups III-IV are distinct from the inventions of Groups I-II and V because these inventions have different modes of operations. The inventions of Groups III-IV are directed to a process that includes active method steps that are different from those recited in the inventions of Groups I-II and V. The inventions of Groups III-IV is a process directed at the treatment of a disease by the removal of cells, treating the cells with a intermediary metabolite or a reagent, and transferring the cells back to the host. The inventions of Groups III-IV is directed to an *ex vivo* treatment technique; whereas the inventions of Groups I-II and V is directed at in *in vivo* use treatment technique. These two techniques are recognized in the art as having a separate status in the art, as evidenced by the different class and subclass assigned to the corresponding sets of groups.

In response to the restriction requirement set forth in the previous office action, Applicant further traversed the restriction requirement among cancer, infection and immune dysfunction. Applicant argues that the subject matter of the Groups focuses on administering a metabolite and a search for the use of a metabolite will encompass several diseases including by not limited to cancer, infection (viral and bacterial), and immune dysfunction.

Applicant's submission has been considered, however, it is not found persuasive. In the instant, a search for a population that is infected with a cancer would not overlap with a population infected with a bacteria or virus. Each of these different diseases is

directed to a specific population of subjects. And a search for a population having a bacterial infection does not necessarily overlap with a population having a viral infection. A search for all populations would impose a serious burden on the Office.

Additionally, Applicant asserts that a restriction requirement among HBV, HCV and HIV is inappropriate because the viruses share a common structure and function in accordance to *In re Harnish*.

Applicant's submission has been considered, however, it is not found persuasive. Contrary to Applicant's submission, HBV, HCV and HIV do not share a common structure. HBV, HCV and HIV do not even belong to the same family of viruses.

HBV is a member of the *Hepadnavirus* family. It consists of a proteinaceous core particle containing the viral genome in the form of double stranded DNA with single-stranded regions and an outer lipid-based envelope with embedded proteins. The envelope proteins are involved in viral binding and release into susceptible cells. The inner capsid relocates the DNA genome to the cell's nucleus where viral mRNAs are transcribed. Three subgenomic transcripts encoding the envelope proteins are made, along with a poorly understood transcript encoding the X protein, whose function is still under debate. A fourth pre-genomic RNA is transcribed, which is exported to the cytosol and translates the viral polymerase and core proteins. Polymerase and pre-genomic RNA are encapsidated in assembling core particles, where reverse transcription of the pre-genomic RNA to genomic DNA occurs by the polymerase protein. The mature core particle then exits the cell via normal secretory pathways, acquiring an envelope along the way

HCV is a positive, single-stranded RNA virus in the *Flaviviridae* family. The genome is approximately 10,000 nucleotides and encodes a single polyprotein of about 3,000 amino acids. The polyprotein is processed by host cell and viral proteases into three major structural proteins and several non-structural protein necessary for viral replication.

And HIV is a member of the genus *lentivirus*, part of the family of retroviridae. Lentiviruses have many common morphologies and biological properties. Many species are infected by lentiviruses, which are characteristically responsible for long duration illnesses associated with a long period of incubation. Lentiviruses are transmitted as single-stranded, positive-sense, enveloped RNA viruses. Upon infection of the target-cell, the viral RNA genome is converted to double-stranded DNA by a virally encoded reverse transcriptase which is present in the virus particle. This viral DNA is then integrated into the cellular DNA for replication using cellular machinery. Once the virus enters the cell, two pathways are possible: either the virus becomes latent and the infected cell continues to function or the virus becomes active, replicates and a large number of virus particles are liberated which can infect other cells.

In the instant, the viruses do not have significant structural similarity as Applicant asserted. Thus, Applicant's submission is not found persuasive. Therefore, because of the reason(s) set forth above, the requirement is still deemed proper and is therefore made **FINAL**.

Status of Claims

2. Claims 1-62 are pending. Claims 1-49 and 61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 08/02/2005. Claims 50-60 and 62 are under examination.

Information Disclosure Statement

3. The information disclosure statement filed 12/19/2003 has been considered in part. The documents listed under the U.S. Patent Documents are not considered, because the document numbers listed therein do not correspond to any U.S. Patent document.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Priority

4. It is noted that this application appears to claim subject matter disclosed in prior Application No. 10/375906, filed 02/27/2003. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For

benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was

unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 50-60 and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In Genentech *Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The broadest independent claim is directed at a process for treating a disease in a mammalian subject comprising the administration of an effective amount of a mammalian metabolite to the subject to modulate or change at least one component of the immune system in said subject. The claims later limit the disease to HCV, claim 60.

The breadth of the claims encompasses a process for the treatment of **all diseases** for all mammalian subjects by perturbing immunoparameters with the administration of any **known metabolites**.

The specification does not contain any working examples. The specification does not set forth any guidelines relating to the type of immune modulation or

perturbation that is necessary to treat the mammalian subject of diseases. The specification does not contain any guidance relating to a single metabolite that is useful in treating a disease that affects mammalian subjects. The specification does not contain evidence suggesting or demonstrating that the administration of a metabolite treats a mammalian subject of any diseases.

All that is noted in the specification is an association between the Gaucher's disease and Hepatitis C virus infection. In the specification, Applicant notes that subjects diagnosed with Gaucher's disease and HCV infection have an immune profile that is different from those diagnosed with only Gaucher's disease, all of which is summarized in Figures 1-6 in the specification. Specifically, Applicant notes the following: i) HCV specific T cell proliferation and the percent of peripheral natural killer T lymphocytes are less in subjects diagnosed with both Gaucher's disease and HCV infection compared to those diagnosed with only Gaucher's disease; and ii) the level of interferon gamma, interleukin-10, interleukin-4 observed in subjects diagnosed with both Gaucher's disease and HCV are higher than those diagnosed with only Gaucher's disease. In the instant, at the very best, the specification sets forth a nexus among various immune parameters, HCV and Gaucher's disease. The specification does not set forth any guidance that would bridge the gap between the observations made by Applicant in the specification and the claimed invention. There is no information provided in the specification pertaining to the type of immune parameter that should be modulated to treat a disease. There is no information provided in the specification regarding the specific immune parameter that a particular metabolite modulates. No

such information or guidance is provided in the specification. In the instant, the specification is **fatality defective** for the claimed invention. The skilled artisan cannot rely on the disclosure set forth in the specification to reasonably practice the invention without an undue burden of experimentation.

In order for the skilled artisan to successfully practice the claimed invention, the skilled artisan must ascertain information pertaining to the type of immunoparameter that should be modulated to treat a disease, and the specific metabolite that modulates the modulates the immunoparameter required for the treatment of the disease. In the instant, the attainment of such information would surely bridge the gap between the use of metabolites and its use in treating a disease. However, the information acquisition process would undeniably be an undoubtedly laborious task that includes both undue and blind experimentations. The skilled artisan would have to unduly and blindly experiment with each known disease, immunoparameters and metabolites to establish a relevance each of the listed variables has over the other. At the time of filing of the instant patent application, the art recognizes that there are approximately 800 to 2000 different metabolites assayed in human subjects.[1] Matching the large number of metabolites known to exist in humans is thousands of diseases, not to mention numerous immunoparameters. A search of the literature renders that there are more than 4000 different diseases, as evidenced by the alphabetical listing of diseases compiled by Karolinska Institutet. Karolinska Institutet summarizes that the 4000 plus diseases fall into the following categories: Bacterial Infections and Mycoses, Virus

Diseases, Parasitic Diseases, Neoplasms (Cancer), Musculoskeletal Diseases, Digestive System Diseases, Stomatognathic Diseases, Respiratory Tract Diseases, Otorhinolaryngologic Diseases, Nervous System Diseases, Eye Diseases, Urologic and Male Genital Diseases, Female Genital Diseases and Pregnancy Complications, Cardiovascular Diseases, Hemic and Lymphatic Diseases, Congenital, Hereditary, and Neonatal Diseases and Abnormalities, Skin and Connective Tissue Diseases, Nutritional and Metabolic Diseases, Endocrine Diseases, Immunologic Diseases, Disorders of Environmental Origin/Poisoning, Animal Diseases, Pathological Conditions, Signs and Symptoms, Behavior and Behavior Mechanisms, and Mental Disorders. (A listing of diseases is attached. The complete listing of diseases is retrieved from http://www.mic.ki.se/Diseases/Alphalist.html)

With such a large abundance of information to mine and analyze, the quantity of experimentation that the skilled artisan would have to conduct is endless. And the imposition of endless experiments would unarguably be an undue burden for the skilled artisan.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F. 2d 1557, 1562, 27 USPQ 2d 1510, 1513 (Fed. Cir. 1993).

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[1] Beecher W.C., Metabolic Profiling: Its Role in Biomarker Discovery and Gene Function Analysis,

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Chapter 17: The human metabolome. *Kluwer Academic, 2003.*

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claim 55 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 106 of copending Application No. 10/675980.

Claim 55 of the instant application is directed at a method of for treating a disease in a mammalian subject comprising administering to said subject an effective amount of a mammalian metabolite to modulate or change at least one component in the immune system of said subject, wherein the mammalian metabolite is a glycolipid comprising a monosaccharide ceramide.

Claim 106 of the conflicting patent application is directed at a method for treating a disease in a mammalian subject comprising administering to said subject an effective amount of an intermediary metabolite to modulate or change at least one component in the immune system of said subject, wherein the intermediary metabolite is glucosylceramide or galactosylceramide.

The difference between the two claims is that claim 106 of the conflicting recites the use of a glucosylceramide or galactosylceramide; whereas, claim 55 is directed at the use of a glycolipid comprising a monosaccharide ceramide.

In the instant, the genus glycolipid comprising a monosaccharide ceramide recited in claim 55 is generic for the species glucosylceramide and galactosylceramide.

That is, claim 106 of the conflicting patent application falls entirely within the scope of claim 55. Claim 55 is anticipated by claim 106 of the conflicting patent application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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